

Fig. 1

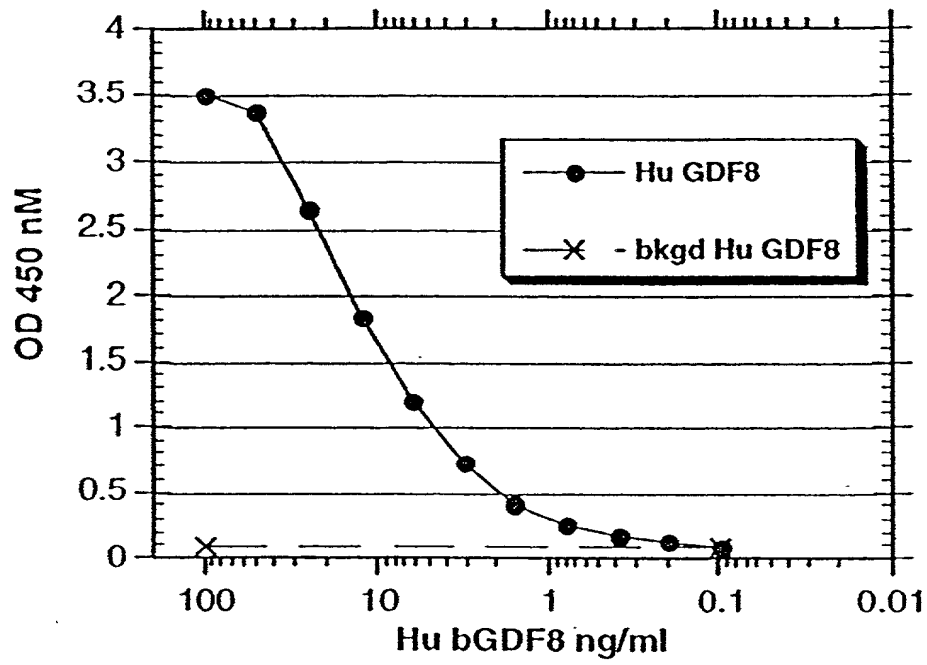


Fig. 2

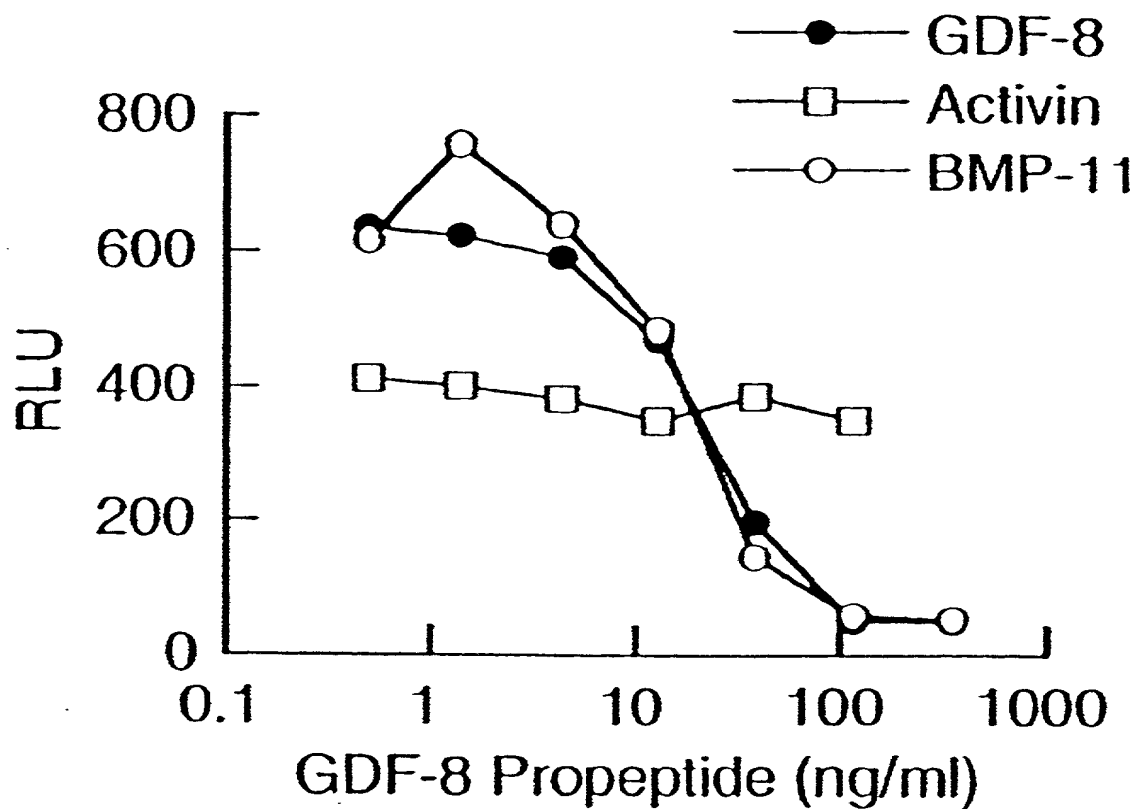


Fig. 3

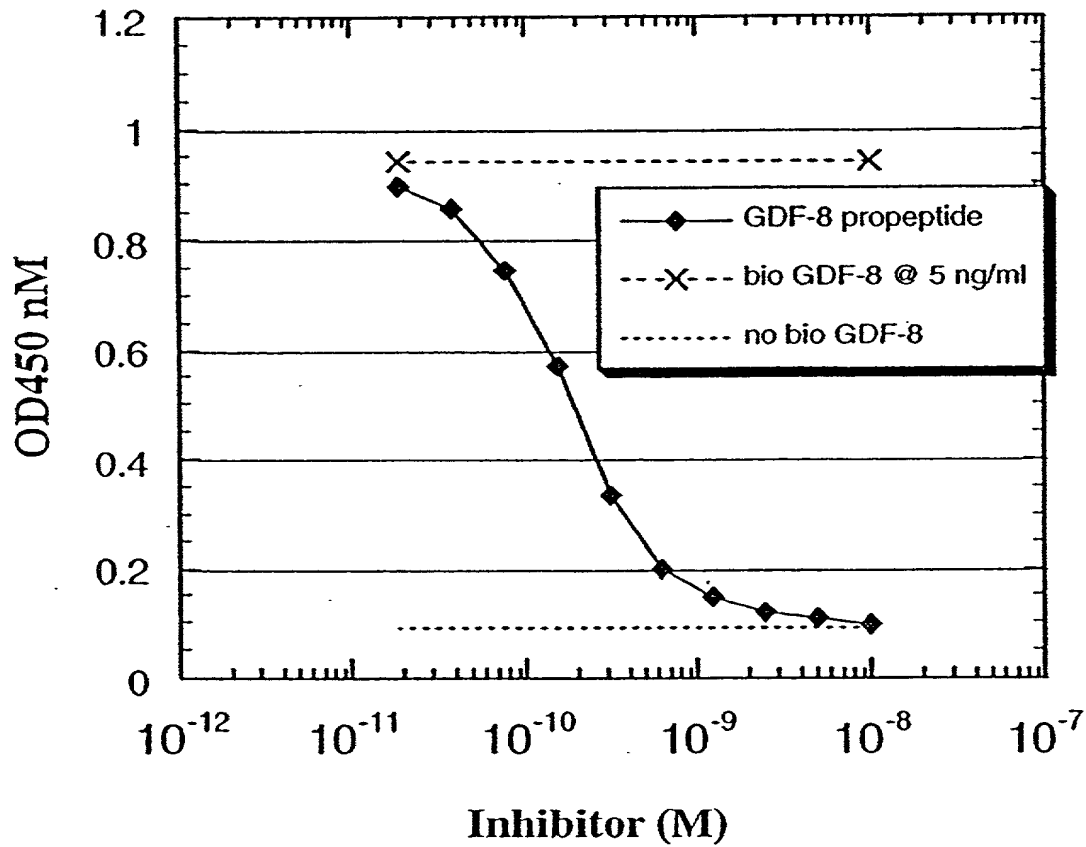


Fig. 4

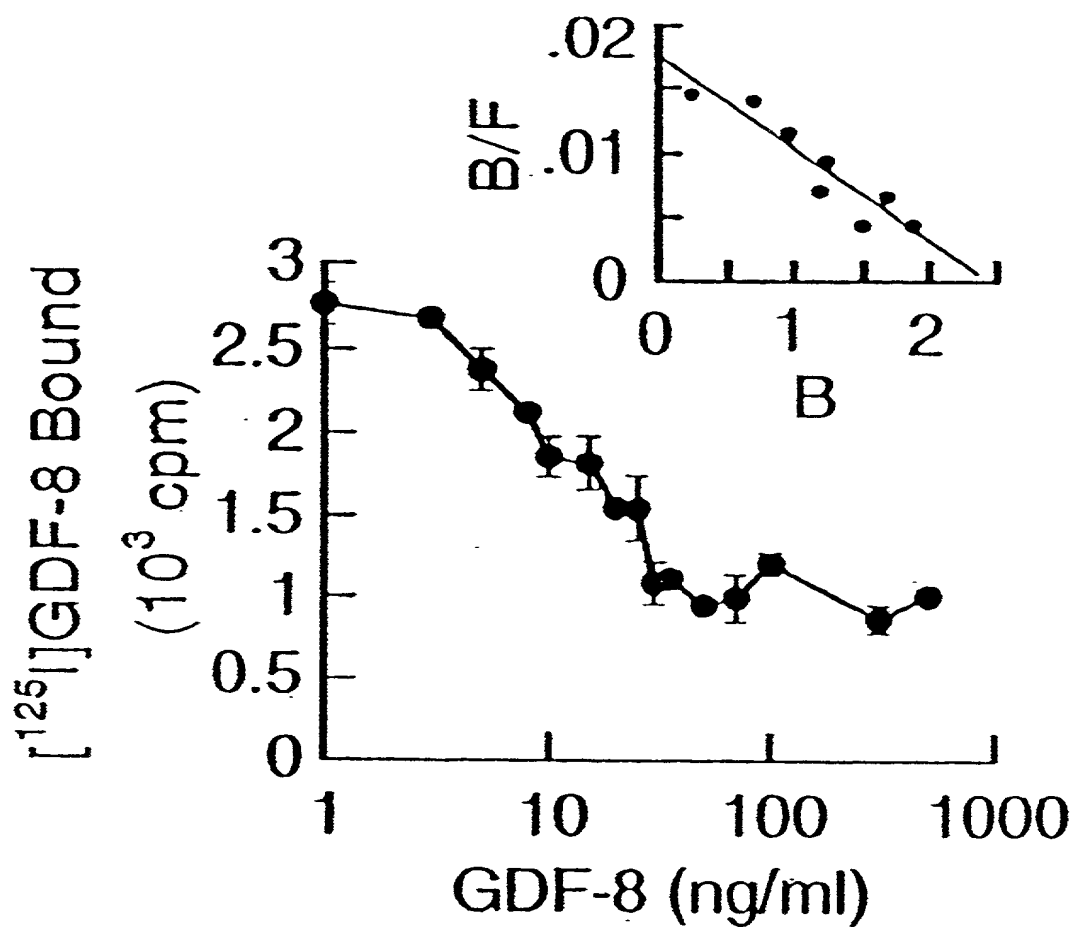


Fig. 5

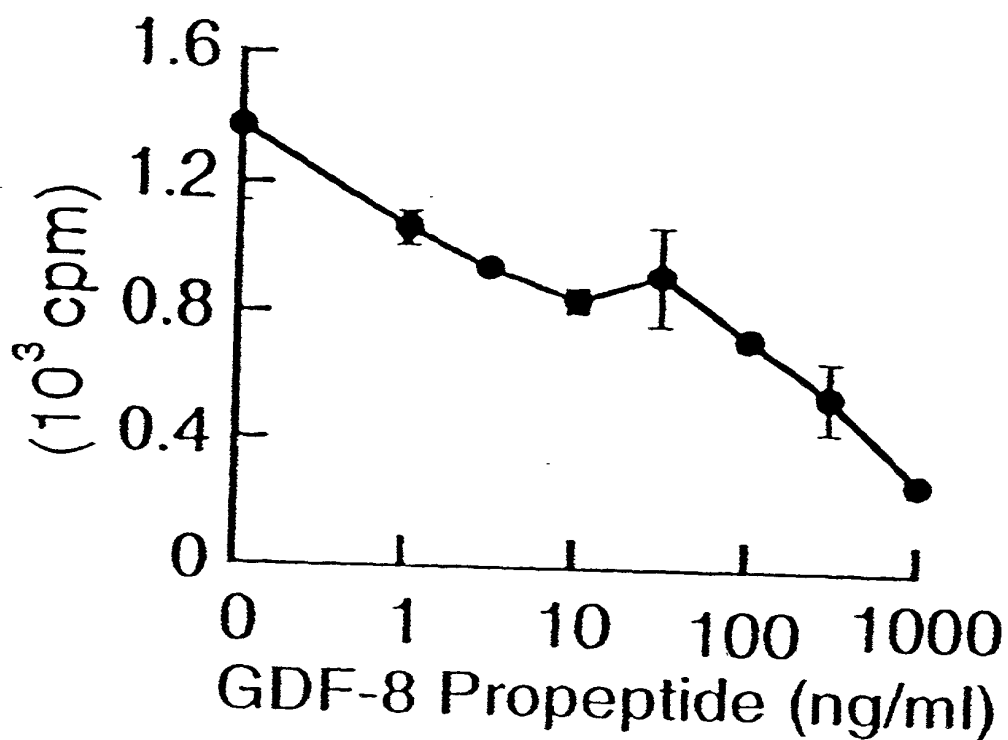


Fig. 6

NEGS	PKRS	EPRG	PGK
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Secretory Mu GDF-8 propeptide Mu IgG2a Fc
 leader

MMQKLQMYVYIYLFMLIAAGPVDLNEGSEEREENVEKEGLCNACAWRQNTSYSRIEAIKIILSKLRLET
 APNISKDAIRQLLPRAPPLRELIDQYDVQRDDSSDGSLEDDEHYHATTETIITMPTESDFLMQADGKPKC
 CFFKFSKKIQYNKVVAQLWIYLRPVKTPTTVFVQILRLIKPMKDGTRYTGIRSLKLDMSGTGIWQSI
 DVKTVLQNLWKQPESNLIGIEIKALDENGHDLA VTFPGGEDGLNPFLEVKVTDTPKRSEPRGPTIKPCP
 PKCPAPNLEGGPSVFIFPPKIKDVLMSLSPIVTCVVDVSEDDPDVQISWFFVNNVEVHTAQQTTHRE
 DYNSTLRVVSALPIQHODWMSGKAFACAVNNKDLPAPIERTISKPKGSVRAPQVYVLPPEEEMTKKQV
 TLTCMVTDFMPEDIYVEWTNNGKTELNYKNTPEVLDSGSYFMYSKLRVEKKNWVERNSYSCSVVHEGL
 HNHHTTKSFSRTPGK

Fig. 7A

NEGS	PKRS	SGS	EPRG	PGK
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Secretory Mu GDF-8 propeptide Mu IgG2a Fc
 leader

MMQKLQMYVYIYLFMLIAAGPVDLNEGSEEREENVEKEGLCNACAWRQNTSYSRIEAIKIILSKLRLET
 APNISKDAIRQLLPRAPPLRELIDQYDVQRDDSSDGSLEDDEHYHATTETIITMPTESDFLMQADGKPKC
 CFFKFSKKIQYNKVVAQLWIYLRPVKTPTTVFVQILRLIKPMKDGTRYTGIRSLKLDMSGTGIWQSI
 DVKTVLQNLWKQPESNLIGIEIKALDENGHDLA VTFPGGEDGLNPFLEVKVTDTPKRSEPRGPTI
 KPCPPCKPAPNLEGGPSVFIFPPKIKDVLMSLSPIVTCVVDVSEDDPDVQISWFFVNNVEVHTAQQTQ
 THREDYNSTLRVVSALPIQHODWMSGKAFACAVNNKDLPAPIERTISKPKGSVRAPQVYVLPPEEEMT
 KKQVTLTCMVTDFMPEDIYVEWTNNGKTELNYKNTPEVLDSGSYFMYSKLRVEKKNWVERNSYSCSVV
 HEGLHNHHTTKSFSRTPGK

Fig. 7B

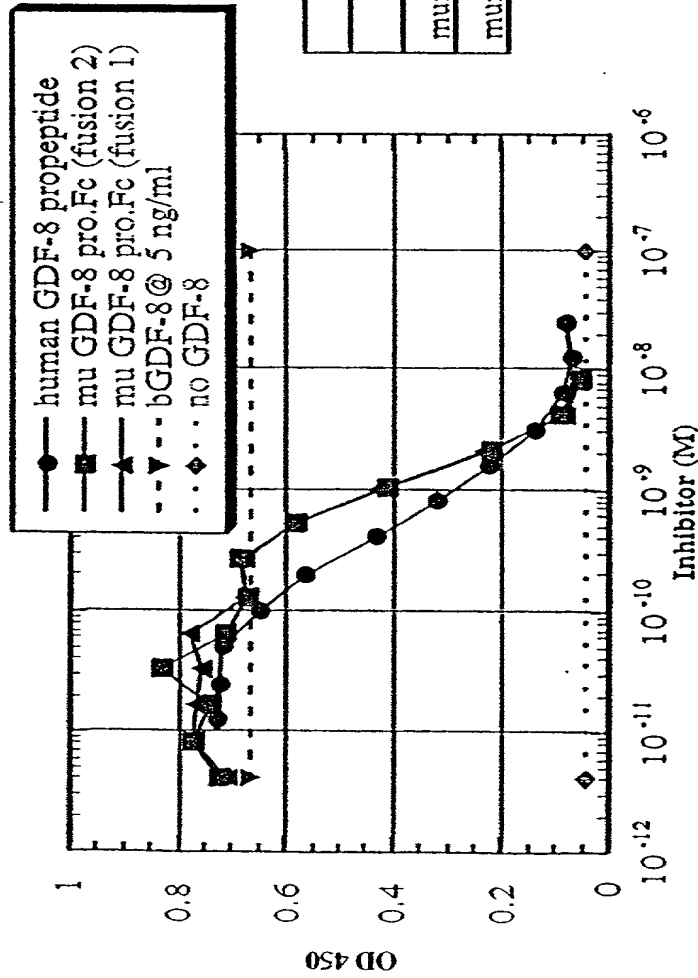


Fig. 8 A

Fig. 8 B

Inhibitor	IC50 (M)
hu GDF-8 propeptide	6 x 10 ⁻¹⁰
murine GDF-8 pro.Fc (Fusion 1)	1.3 x 10 ⁻⁹
murine GDF-8 pro.Fc (Fusion 2)	1.3 x 10 ⁻⁹

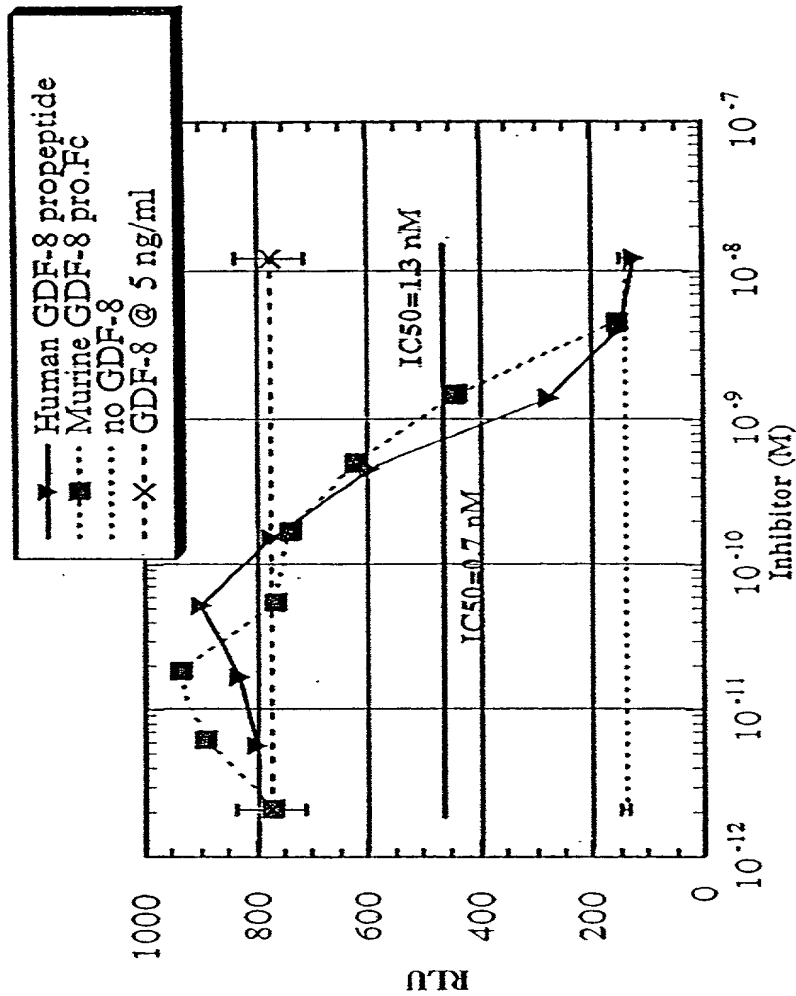


Fig. 9

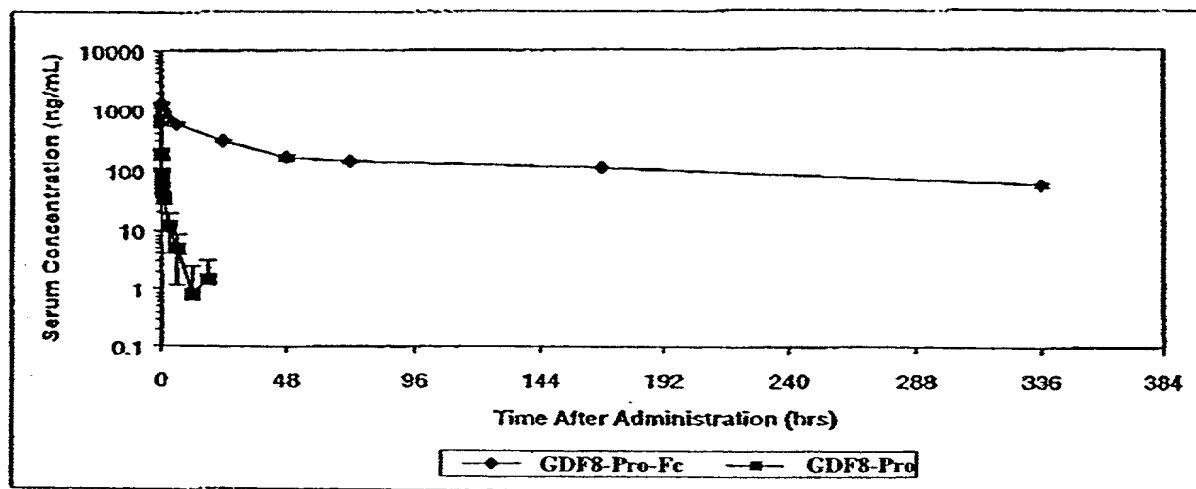


Fig. 10

	NENS	PKRS	EPKS	PGK
Secretory	Hu GDF-8 propeptide			Hu IgG1 Fc
leader				

MQKLQLCVYIYLFMLIVAGPVLDLNENSEQKENVEKEGLCNACTWRQNTKSSRIEAIKIQLSKLRLETAPN
 ISKDVIRQLLPKAPPLRELIDQYDVQRDDSSDGSLEDDDYHATTETIIITMPTESDFLMQVDGKPKCCFFKF
 SSKIQYNKVVKQAQLWIYLRPVETPTTVFVQILRLIKPMKDGTRYTGIRSLKLDMPGTGIWQSIDVKTVLQ
 NWLKPESNLGIEIKALDENGHDLAFTFPGGEDGLNPFLEVKVTDTPKRSEPKSCDKTHTCPPCPAPELL
 GGPSVFLFPPKPKDTLMISRTPETCVVDVSHEDPEVKFNWYVDGVEVHNATKTPREEQYNSTYRVVSVL
 TVLHQDWLNGKEYCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREEMTKNQVSLTCLVKGFYPSDI
 AVEWESNGQPENNYKTTTPPVLDSDGSFFLYSKLTVDKSRWQQGNVFCSVMEALHNHYTQKSLSLSPGK

Fig. 11A

	NENS	PKRS	DKT	PGK
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Secretory leader Hu GDF-8 propeptide Hu IgG1 Fc mutated

MQKLQLCVYIYLFMLIVAGPVVDLNNENSEQKENVEKEGLCNACTWRQNTKSSRIEAIKIQILSKLRLETAPN
 ISKDVIRQLLPKAPPLRELIDQYDVQRDDSSDGSLEDDDYHATTETIITMPTESDFLMQVDGKPKCCFFKF
 SSKIQYNKVVKAKLWIYLRPVETPTTVFVQILRLIKPMKDGTRYTGIRSLKLDNMPGTGIWQSIDVKTVLQ
 NWLKQPESNLGIKALDENNGHDLAVTFPPGPGEDGLNPFLEVKVTDTPKRS~~DK~~TH~~TC~~PPCPAPEALGAPS~~V~~
 FLFPKPKD~~TL~~MISRTPEVTCVVVDVSHEDPEVKFNWYVDGVEVHNAKTKPREEQYNSTYRVVSVLT~~VL~~HQ
 DWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREEMTKNQVSLTCLVKGFYPSDIAVEWE
 SNGQPENNYKTTTPPVLDSDGSFFLYSKLTVDKSRWQQGNV~~FS~~CSVMHEALHNHYTQKSLSLSPGK

Fig. 11B

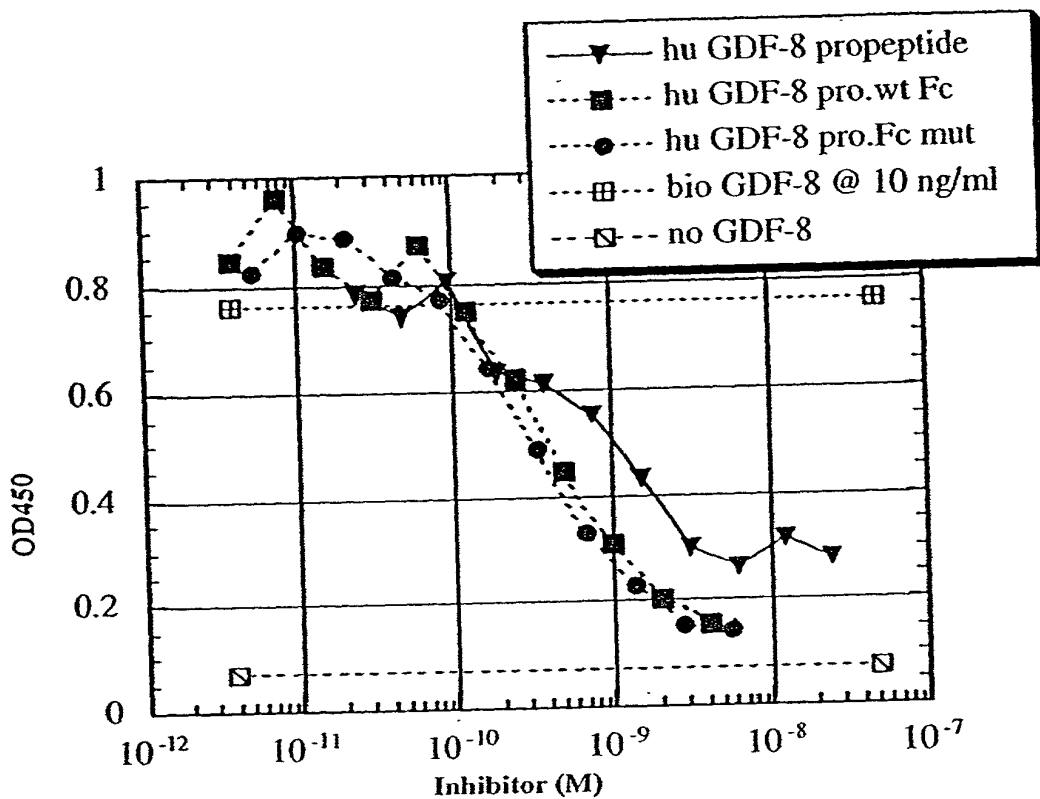


Fig. 12

Dissected Tissue Mass

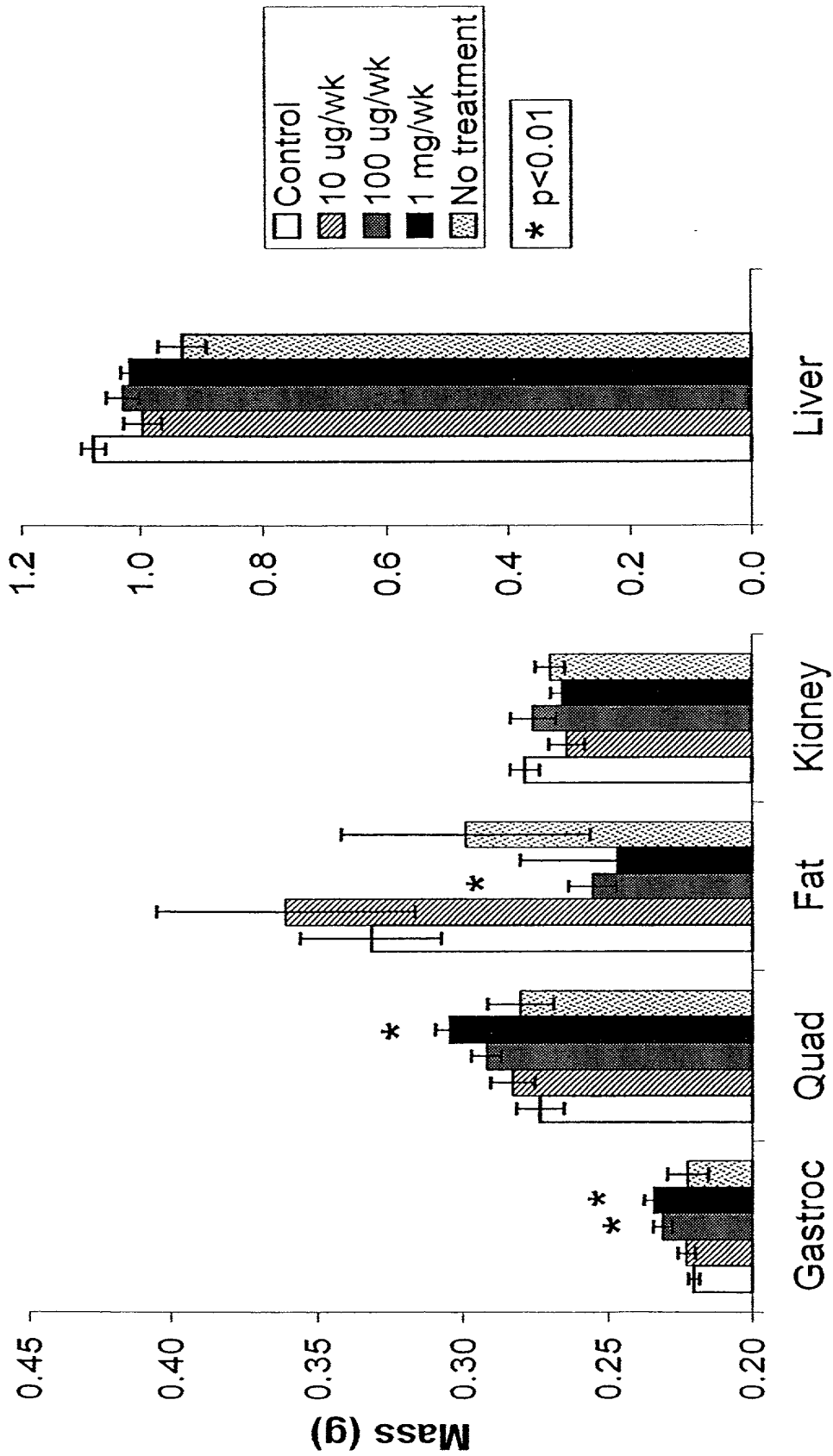


Figure 13

Fig. 14A

SEQ ID NO:1 Human GDF-8 precursor protein - protein
sequence

MQKLQLCVYIYLFMLIVAGPVDLNENSEQKENVEKEGLCNACTWRQNTKSS
RIEAIKIQILSKLRLETAPNISKDVIRQLLPKAPPLRELIDQYDVQRDDSS
DGSLEDDDYHATTETIITMPTESDFLMQVDGKPKCCFFKFSSKIQYNKVVK
AQLWIYLRPVETPTTVFVQILRLIKPMKDGTTRYTGIRSLKLDMPGTGIWQ
SIDVKTVLQNLWKQPESNLGIEIKALDENGHDLAFTFPGPGEDGLNPFLEV
KVTDTPKRSRRDFGLDCDEHSTESRCCRYPLTVDFEAFGWDWI IAPKRYKA
NYCSGECEFEVFLQKYPHTLVHQANPRGSAGPCCTPTKMSPINMLYFNGKE
QIIYGKIPAMVVDRCGCS

Fig. 14B

SEQ ID NO:2 Human GDF-8 precursor protein - DNA
sequence

ATGCAAAACTGCAACTCTGTGTTTATATTTACCTGTTTATGCTGATTGT
TGCTGGTCCAGTGGATCTAAATGAGAACAGTGAGCAAAAAGAAAATGTGG
AAAAAGAGGGGCTGTGTAATGCATGTACTTGGAGACAAAACACTAAATCT
TCAAGAATAGAAGCCATTAAGATACAAATCCTCAGTAAACTTCGTCTGGA
AACAGCTCCTAACATCAGCAAAGATGTTATAAGACAACTTTTACCCAAAG
CTCCTCCACTCCGGGAACTGATTGATCAGTATGATGTCCAGAGGGATGAC
AGCAGCGATGGCTCTTTGGAAGATGACGATTATCACGCTACAACGGAAAC
AATCATTACCATGCCTACAGAGTCTGATTTTCTAATGCAAGTGGATGGAA
AACCCAAATGTTGCTTCTTTAAATTTAGCTCTAAAATACAATACAATAAA
GTAGTAAAGGCCCAACTATGGATATATTTGAGACCCGTCGAGACTCCTAC
AACAGTGTTTTGTGCAAATCCTGAGACTCATCAAACCTATGAAAGACGGTA
CAAGGTATACTGGAATCCGATCTCTGAAACTTGACATGAACCCAGGCACT
GGTATTTGGCAGAGCATTGATGTGAAGACAGTGTTGCAAAATTGGCTCAA
ACAACCTGAATCCAACCTTAGGCATTGAAATAAAAGCTTTAGATGAGAATG
GTCATGATCTTGCTGTAACCTTCCCAGGACCAGGAGAAGATGGGCTGAAT
CCGTTTTTTAGAGGTCAAGGTAACAGACACACCAAAAAGATCCAGAAGGGA
TTTTTGGTCTTGACTGTGATGAGCACTCAACAGAATCACGATGCTGTCGTT
ACCCTCTAACTGTGGATTTTGAAGCTTTTGGATGGGATTGGATTATCGCT
CCTAAAAGATATAAGGCCAATTACTGCTCTGGAGAGTGTGAATTTGTATT
TTTACAAAAATATCCTCATACTCATCTGGTACACCAAGCAAACCCAGAG
GTTTCAGCAGGCCCTTGCTGTACTCCCACAAAGATGTCTCCAATTAATATG
CTATATTTTAATGGCAAAGAACAAATAATATATGGGAAAATTCCAGCGAT
GGTAGTAGACCGCTGTGGGTGCTCA

Fig. 14C

SEQ ID NO:3 Human mature GDF-8 - protein sequence

DFGLDCDEHSTESRCCRYPLTVDFEAFGWDWIIAPKRYKANYCSGECEVFV
LQKYPHTHLVHQANPRGSAGPCCTPTKMSPINMLYFNGKEQIIYGKIPAMV
VDRCGCS

Fig. 14D

SEQ ID NO:4 Human mature GDF-8 - DNA sequence

GATTTTGGTCTTGACTGTGATGAGCACTCAACAGAATCACGATGCTGTCTCG
TTACCCTCTAACTGTGGATTTTGAAGCTTTTGGATGGGATTGGATTATCG
CTCCTAAAAGATATAAGGCCAATTACTGCTCTGGAGAGTGTGAATTTGTA
TTTTTACAAAAATATCCTCATACTCATCTGGTACACCAAGCAAACCCAG
AGGTTTCAGCAGGCCCTTGCTGTACTCCACAAAGATGTCTCCAATTAATA
TGCTATATTTTAATGGCAAAGAACAAATAATATATGGGAAAATTCCAGCG
ATGGTAGTAGACCGCTGTGGGTGCTCA

Fig.14E

SEQ ID NO:5 Human GDF-8 propeptide - protein
sequence

NENSEQKENVEKEGLCNACTWRQNTKSSRIEAIKIQILSKLRLETAPNISK
DVIRQLLPKAPPLRELIDQYDVQRDDSSDGSLEDDDYHATTETIITMPTES
DFLMQVDGKPKCCFFKFSSKIQYNKVVKAAQLWIYLRPVETPTTVFVQILRL
IKPMKDGYTRYTGIRSLKLDMNPGTGIWQSIDVKTVLQNLKQPESNLGIEI
KALDENGHDLAVTFPGPGEDGLNPFLEVKVTDTPKRSRR

Fig. 14F

SEQ ID NO:6 Human GDF-8 propeptide - DNA sequence

AATGAGAACAGTGAGCAAAAAGAAAATGTGGAAAAAGAGGGGCTGTGTAAT
GCATGTACTTGGAGACAAAACACTAAATCTTCAAGAATAGAAGCCATTAAG
ATACAAATCCTCAGTAACTTTCGTCTGGAAACAGCTCCTAACATCAGCAAA
GATGTTATAAGACAACCTTTTACCCAAAGCTCCTCCACTCCGGGAACTGATT
GATCAGTATGATGTCCAGAGGGATGACAGCAGCGATGGCTCTTTTGAAGAT
GACGATTATCACGCTACAACGGAAACAATCATTACCATGCCTACAGAGTCT
GATTTTCTAATGCAAGTGGATGGAAAACCCAAATGTTGCTTCTTTAAATTT
AGCTCTAAAATACAATAACAATAAAGTAGTAAAGGCCCAACTATGGATATAT
TTGAGACCCGTCGAGACTCCTACAACAGTGTGTTGTGCAAATCCTGAGACTC
ATCAAACCTATGAAAGACGGTACAAGGTATACTGGAATCCGATCTCTGAAA
CTTGACATGAACCCAGGCACTGGTATTTGGCAGAGCATTGATGTGAAGACA
GTGTTGCAAAATTGGCTCAAACAACCTGAATCCAACCTTAGGCATTGAAATA
AAAGCTTTAGATGAGAATGGTCATGATCTTGCTGTAACCTTCCCAGGACCA
GGAGAAGATGGGCTGAATCCGTTTTTTAGAGGTCAAGGTAACAGACACACCA
AAAAGATCCAGAAGG

Fig. 14G

SEQ ID NO:7 Human BMP-11 precursor protein -
protein sequence

MVLAAPLLLGLLLALELRPRGEAAEGPAAAAAAAAAAAAAGVGGERSSRP
APSVAPEPDGCPVCVWRQHSRELRLSEIKSQILSKLRLKEAPNISREVVKQ
LLPKAPPLQQILDLHDFQGDALQPEDFLEEDEYHATTETVISMASETDP
QTDGSPLCCHFHFSPKVMFTKVLKAQLWVYLRPVPRPATVYLLQILRLKPLT
GEGTAGGGGGRRHIRIRSLKIELHSRSGHWQSIDFKQVLHSWFRQPQSNW
GIEINAFDPSGTDLAVTSLGPGAEGLPFMELRVLENTKRSRRNLGLDCDE
HSSESRCRYPLTVDFEAFGWDWIIAPKRYKANYCSGQCEYMFQKYPHTH
LVQQANPRGSAGPCCTPTKMSPINMLYFNDKQQIIYGKIPGMVVDRCGS

Fig. 14H

SEQ ID NO:8 Human BMP-11 precursor protein - DNA
sequence

ATGGTGCTCGCGGCCCCGCTGCTGCTGGGCTTCCTGCTCCTCGCCCTGGA
GCTGCGGCCCCGGGGGGAGGCGGCCGAGGGCCCCGCGGCGGCGGCGGCGG
CGGCGGCGGCGGCGGCAGCGGCGGGGGTGGGGGGGAGCGCTCCAGCCGG
CCAGCCCCGTCCGTGGCGCCCCGAGCCGGACGGCTGCCCCGTGTGCGTTTG
GCGGCAGCACAGCCGCGAGCTGCGCCTAGAGAGCATCAAGTCGCAGATCT
TGAGCAAACCTGCGGCTCAAGGAGGCGCCCAACATCAGCCGCGAGGTGGTG
AAGCAGCTGCTGCCCAAGGCGCCGCCGCTGCAGCAGATCCTGGACCTACA
CGACTTCCAGGGCGACGCGCTGCAGCCCGAGGACTTCCTGGAGGAGGACG
AGTACCACGCCACCAACCGAGACCGTCATTAGCATGGCCCAGGAGACGGAC
CCAGCAGTACAGACAGATGGCAGCCCTCTCTGCTGCCATTTTCACTTCAG
CCCCAAGGTGATGTTACAAAGGTACTGAAGGCCAGCTGTGGGTGTACC
TACGGCCTGTACCCCGCCAGCCACAGTCTACCTGCAGATCTTGCGACTA
AAACCCCTAACTGGGGAAGGGACCGCAGGGGGAGGGGGCGGAGGCCGGCG
TCACATCCGTATCCGCTCACTGAAGATTGAGCTGCACTCACGCTCAGGCC
ATTGGCAGAGCATCGACTTCAAGCAAGTGCTACACAGCTGGTTCCGCCAG
CCACAGAGCAACTGGGGCATCGAGATCAACGCCTTTGATCCCAGTGGCAC
AGACCTGGCTGTACCTCCCTGGGGCCGGGAGCCGAGGGGGCTGCATCCAT
TCATGGAGCTTTCGAGTCCTAGAGAACACAAAACGTTCCCGGCGGAACCTG
GGTCTGGACTGCGACGAGCACTCAAGCGAGTCCCGCTGCTGCCGATATCC
CCTCACAGTGGACTTTGAGGCTTTCGGCTGGGACTGGATCATCGCACCTA
AGCGCTACAAGGCCAACTACTGCTCCGGCCAGTGCGAGTACATGTTTCATG
CAAAAATATCCGCATACCCATTTGGTGCAGCAGGCCAATCCAAGAGGCTC
TGCTGGGCCCTGTTGTACCCCCACCAAGATGTCCCAATCAACATGCTCT
ACTTCAATGACAAGCAGCAGATTATCTACGGCAAGATCCCTGGCATGGTG
GTGGATCGCTGTGGCTGCTCT

Fig. 14I

SEQ ID NO:9 Human BMP-11 mature - protein sequence

NLGLDCDEHSSESRCRYPLTVDFEAFGWDWI IAPKRYKANYCSGQCEYMF
MQKYPHTHLVQQANPRGSAGPCCTPTKMSPINMLYFNDKQQIIYGKIPGMV
VDRCGCS

Fig. 14J

SEQ ID NO:10 Human BMP-11 mature - DNA sequence

AACCTGGGTCTGGACTGCGACGAGCACTCAAGCGAGTCCCGCTGCTGCCG
ATATCCCCCTCACAGTGGACTTTGAGGCTTTCGGCTGGGACTGGATCATCG
CACCTAAGCGCTACAAGGCCAACTACTGCTCCGGCCAGTGCGAGTACATG
TTCATGCAAAAATATCCGCATACCCATTTGGTGCAGCAGGCCAATCCAAG
AGGCTCTGCTGGGCCCTGTTGTACCCCCACCAAGATGTCCCCAATCAACA
TGCTCTACTTCAATGACAAGCAGCAGATTATCTACGGCAAGATCCCTGGC
ATGGTGGTGGATCGCTGTGGCTGCTCT

Fig. 14K

SEQ ID NO:11 Human BMP-11 propeptide - protein
sequence

AEGPAAAAAAAAAAAAAGVGGERSSRPAPSVAPDPGCPVCVWRQHSRELR
LESIKSQILSKLRLKEAPNISREVVKQLLPKAPPLQQILDLHDFQGDALQP
EDFLEEDEYHATTETVISMAQETDPAVQTDGSPLCCHFHFSPKVMFTKVLK
AQLWVYLRPVPRPATVYLQILRLKPLTGEGTAGGGGGGRRHIRIRSLKIEL
HSRSGHWQSIDFKQVLHSWFRQPQSNWGIEINAFDPSGTDLAVTSLGPGAE
GLHPFMELRVLENTKRSRR

SEQ ID NO:12 Human BMP-11 propeptide - DNA
sequence

[illegible]

Fig. 14M

SEQ ID NO:13 GDF-8 signal sequence - protein sequence

MQKLQLCVYIYLFMLIVAGPVDL

Fig. 14N

SEQ ID NO:14 BMP-11 signal sequence - protein
sequence

MVLAAPLLLGFLLLALELRPRGEA

Fig. 14Q

SEQ ID NO:15 Human IgG1-Fc - protein sequence

EPKSCDKTHTCPPCPAPELLGGPSVFLFPPKPKDTLMISRTPEVTCVVVDV
SHEDPEVKFNWYVDGVEVHNAKTKPREEQYNSTYRVVSVLTVLHQDWLNGK
EYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREEMTKNQVSLTCL
VKGFYPSDIAVEWESNGQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWQQ
GNVFSCSVMHEALHNHYTQKSLSLSPGK

Fig. 14P

SEQ ID NO:16 Human IgG1-Fc modified - protein
sequence

DKTHTCPPCPAPEALGAPSVFLFPPKPKDTLMISRTPEVTCVVVDVSHEDP
EVKFNWYVDGVEVHNAKTKPREEQYNSTYRVVSVLTVLHQDWLNGKEYKCK
VSNKALPAPIEKTISKAKGQPREPQVYTLPPSREEMTKNQVSLTCLVKGFY
PSDIAVEWESNGQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWQQGNVFS
CSVMHEALHNHYTQKSLSLSPGK